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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte DAVID E. WOLF and DYLAN A. BULSECO

Appeal 2009-014065
Application 10/632,725
Technology Center 1600

Before, CAROL A. SPIEGEL, TONI R. SCHEINER and STEPHEN WALSH, *Administrative Patent Judges*.

WALSH, *Administrative Patent Judge*.

DECISION ON APPEAL[1]

This is an appeal under 35 U.S.C. § 134(a) involving claims to a method of assaying for a pathogen. We have jurisdiction under 35 U.S.C. § 6(b). We affirm-in-part.

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[1] The two-month time period for filing an appeal or commencing a civil action, as recited in 37 C.F.R. § 1.304, or for filing a request for rehearing, as recited in 37 C.F.R. § 41.52, begins to run from the "MAIL DATE" (paper delivery mode) or the "NOTIFICATION DATE" (electronic delivery mode) shown on the PTOL-90A cover letter attached to this decision.

STATEMENT OF THE CASE

Appellants state that claims 59-66 and 118-138 are on appeal. (App. Br. 5.) Claim 59 illustrates the subject matter:

59. A method of assaying for a pathogen in a sample, said method comprising:
exciting said sample with radiation, said sample comprising
at least one pathogen;
at least one probe, and
at least one fluorescent tag;
measuring the fluorescence from a subvolume of said excited sample; and
analyzing the fluctuations of said fluorescence that are due to the diffusion or flow of said pathogen through said subvolume.

The Examiner rejected the claims as follows:

- claims 132-137 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement because they include new matter;

- claims 59, 118-121, 124-126, 130-132, 134 and 136 under 35 U.S.C. § 112, 2nd paragraph, as indefinite because claim 59 omits an essential step;

- claims 131-133 under 35 U.S.C. § 112, 2nd paragraph, as indefinite because claim 131 recites the term "unknown" and because claims 132 and 133 recite "a period of seconds;"

- claims 59-66, 118-125, 127, 128, 130-133 and 138 under 35 U.S.C. § 102(e) as anticipated by Rigler et al., US 6,582,903 B1[2] ("Rigler '903");

[2] Rudolf Rigler et al., US 6,582,903 B1, filed Feb. 10, 1998, issued Jun. 24, 2003.

• claims 59-64, 66, 118-125, 127, 128, 130-133 and 138 under 35 U.S.C. § 102(b) as anticipated by Rigler, Journal of Biotechnology[3] ("Rigler 1995");

• claims 59-64, 66, 118-125, 127, 128 and 130-138 under 35 U.S.C. § 102(b) as anticipated by Weiner;[4]

• claims 59-65, 118-125, 127, 128 and 130-138 under 35 U.S.C. § 102(b) as anticipated by Walter;[5] and

• claims 59-66, 118-125, 127, 128 and 130-138 under 35 U.S.C. § 103(a) as unpatentable over Kask[6] and Lahiri.[7]

NEW MATTER

The Issue

The Examiner's position is that "[c]laims 132-137 state limitations drawn to analyzing occurring over particular ranges of seconds [but] these limitations do not appear to find support in the specification as filed." (Ans. 4.)

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[3] Rudolf Rigler, *Fluorescence correlations, single molecule detection and large number screening Applications in biotechnology*, 41 J. BIOTECH. 177-186 (1995).

[4] Olaf H. Weiner et al., *Rapid and Reproducible Quantification of Hepatitis C Virus cDNA by Fluorescence Correlation Spectroscopy*, 61 DIGESTION 84-89 (2000).

[5] Nils G. Walter et al., *Fluorescence correlation analysis of probe diffusion simplifies quantitative pathogen detection by PCR*, 93 PROC. NATL. ACAD. SCI. USA 12805-12810 (1996).

[6] Peet Kask, US 6,515,289 B1, filed Dec. 10, 1999, issued Feb. 4, 2003.

[7] Joydeep Lahiri et al., Pub. No. US 2003/0138853 A1, filed Jan. 13, 2003, published Jul. 24, 2003.

Appellants contend that "Examples 1-4 and FIGS. 1A, 2A 3A and 4A of the [] application provide examples of the requisite support." (App. Br. 11.) According to Appellants, Example 1 and FIG. 1A support "over a period of seconds;" Example 2 and FIG. 2A support "a period of less than 30 seconds;" and Example 4 and FIG. 4A support "a period of less than 15 seconds." (*Id.*)

The issue with respect to this rejection is whether the time periods set forth in claims 132-137 were disclosed in Appellants' original Specification.

Findings of Fact

1. FIG. 1A displays plots of data collected in two channels over a range of seconds, the horizontal axis of the plot labeled "Time (s)", with marks ticked at increments of five from 0 to 65, and numerical labels at increments of ten from 0 to 60.
2. FIG. 2A has horizontal axis time markings similar to FIG. 1A.
3. FIG. 4A displays a plot having a horizontal axis labeled "Time (s)", with marks ticked at increments of 2.5 from 0 to 35, and numerical labels at increments of five 0 to 35.

Principles of Law

"If . . . the specification contains a description of the claimed invention, albeit not *in ipsis verbis* (in the identical words), then the examiner . . ., in order to meet the burden of proof, must provide reasons why one of ordinary skill in the art would not consider the description sufficient." *In re Alton*, 76 F.3d 1168, 1175 (Fed. Cir. 1996). "[U]nder proper circumstances, drawings alone may provide a 'written description' of an invention as required by § 112." *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1565 (Fed. Cir. 1991).

Analysis

Appellants disclosed analysis plots in the original drawings. The plots include the label "Time (s)" on the horizontal axis, and the Examiner does not dispute that the "s" means "seconds." We agree with Appellants that the original drawings disclosed analyzing over a period of seconds, for at least 15 seconds, and for at least 30 seconds. (FF 1-3.) The Examiner dismissed the evidence "because the drawings do not provide support for an open-ended duration of seconds, as claimed" (Ans. 4-5), a point not raised in the original rejection. The plots in the drawings are displayed as far as 60 seconds. We have no information on why the plots were not extended beyond 60 seconds, but in the working Examples given, it appears that relevant perturbations are shown shortly before that point. The law does not require that there be working examples for every limitation claimed, unless a reason for the requirement is shown. The Examiner did not provide reasons why one of ordinary skill in the art would find the disclosure insufficient for an "open-ended" observation period. The rejection therefore did not meet the burden of proof for the "open-ended" issue. *See Alton*, 76 F.3d at 1175.

DEFINITENESS

Principles of Law

"The test for definiteness is whether one skilled in the art would understand the bounds of the claim when read in light of the specification." *Miles Laboratories Inc. v. Shandon Inc.*, 997 F.2d 870, 875 (Fed. Cir. 1993).

A. Claim 59

The Issues

The Examiner's positions are: (1) claim 59 omits the essential step "determining the presence or absence of the pathogen;" (2) claim 59 is

indefinite "because it is unclear that the method steps are for the method as set forth in the preamble;" and (3) the problem could be cured by adding the words "thereby assaying for a pathogen in the sample," which the Examiner characterized as a "final step." (Ans. 5-6.)

Appellants contend that (1) "the method steps set forth in claim 59 are for the method recited in the preamble—they could be for no other method;" and (2) the Examiner's proposed amendment "phrase is not necessary." (App. Br. 13-14.)

The issues with respect to this rejection are:

whether claim 59 omits an essential step; and

whether it is unclear that the steps are for the method set forth in the preamble.

Analysis

In plain language, the claimed method assays for a pathogen by analyzing fluorescence fluctuations that are "due to the diffusion of flow of said pathogen." If a pathogen isn't there, there won't be fluctuations due to the pathogen. We therefore do not agree with the Examiner that determining the presence or absence of the pathogen is an omitted step.

We agree with Appellants that it is not at all "unclear" that the method steps are for the method set forth in the preamble, as the Examiner argues. Finally, the Examiner's proposed amendment is not a step and it adds no process that is not already there. It merely states what has been accomplished by the actual steps, a fact already apparent in the plain language of the claim. We agree with Appellants that the Examiner's proposed amendment is not necessary.

B. Claim 131 ("wherein the identity of said pathogen is unknown")

The Issue

The Examiner's position is that "it is unclear as to who[m] or what the identity of the pathogen is 'unknown' or the distinguishing physical feature of a pathogen that is unknown," and "unclear as to whether the language refers to a mental step or attempts to refer to a structural limitation of the claimed [sic] product." (Ans. 6.)

Appellants contend that "the term 'unknown' is well-known throughout all fields of science," and "[t]he phrase 'identity of said pathogen is unknown' refers to a fact—not a mental step." According to Appellants, "[t]he identity of the pathogen in the sample is unknown at the time the method is conducted." (App. Br. 14-15.)

The issue for this rejection is whether the Examiner has shown that a person of ordinary skill in the art would not understand the bounds of the claim when read in light of the Specification.

Analysis

We agree with Appellants that the claim uses known terms, that a person of ordinary skill in the art would understand the claim, and that on this record the rejection must be reversed.

C. Claims 132 and 133 ("analyzing occurs over a period of seconds")

The Issue

The Examiner's position is that the limitation wherein the analyzing occurs over a period of seconds "is tantamount to claiming that the analyzing occurs over a period of time, and so would not apprise one of skill in the art of the metes and bounds of the claimed invention." (Ans. 6.)

Appellants contend that "[t]here is nothing indefinite about a second or a period of seconds," and "an analysis that occurs over a plurality of seconds falls within the claim." (App. Br. 15.)

The issue for this rejection is whether the Examiner has shown that a person of ordinary skill in the art would not understand the bounds of the claim when read in light of the Specification.

Analysis

For the reasons stated in Appellants' Brief, we agree with Appellants that the claim uses known terms, that a person of ordinary skill in the art would understand the metes and bounds of the claim, and that on this record the rejection must be reversed.

CLAIM INTERPRETATION – "PATHOGEN"

The meaning of the claim term "pathogen" is disputed in each of the rejections over prior art. We therefore discuss claim interpretation first.

Issue

The Examiner interpreted "pathogen" to mean not only an organism but also a molecule from a pathogenic organism, and found that prior art references assaying for the presence of certain molecules anticipated the claims.

Appellants contest the Examiner's interpretation of "pathogen," arguing that it is not what they intended. For example, when addressing the rejection over Rigler '903, Appellants contend that Rigler '903 sought to analyze single molecules, but the claimed method assays for a pathogen, and "[a] pathogen is an organism." (App. Br. 18.) According to Appellants, the Specification discloses a pathogen as an example of an organism. (*Id.*, citing Spec. 33, ll. 5-6.) "This evidence from the record clearly demonstrates that

Appellants intended the term 'pathogen' to refer to an organism, and to convey the idea that while a pathogen necessarily includes a component of a pathogen, a component of a pathogen is not inherently a pathogen or an organism." (*Id.*) Applying their claim interpretation, Appellants contend that "Rigler et al. must expressly teach analyzing the fluctuations of the fluorescence due to the diffusion or flow of a pathogen through a subvolume to establish a case of *prima facie* anticipation, and they do not." (*Id.* at 19.)

The issue is whether the Examiner correctly interpreted "pathogen" to include not only organisms but also molecules.

Principles of Law

"[T]he specification 'is always highly relevant to the claim construction analysis. Usually, it is dispositive; it is the single best guide to the meaning of a disputed term.'" *Phillips v. AWH Corp.*, 415 F.3d 1303, 1315 (Fed. Cir. 2005) (en banc), *quoting Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996). "Absent claim language carrying a narrow meaning, the PTO should only limit the claim based on the specification or prosecution history when those sources expressly disclaim the broader definition." *In re Bigio*, 381 F.3d 1320, 1325 (Fed. Cir. 2004).

Analysis

The Specification does not support Appellants' argument that only organisms are pathogens. The Specification states:

> In a second aspect, the invention features a method of assaying for the presence of a pathogen component in a sample . . . .
>
> In one embodiment the pathogen component includes a bacterium. In other embodiments the pathogen component includes a virus. In another embodiment the pathogen component is selected from the group consisting of pathogen,

> pathogen fragment, pathogen nucleic acid, pathogen protein, pathogen carbohydrate, and combinations thereof. In some embodiments the pathogen component is selected from the group consisting of pathogen spore, pathogen toxin, metabolic product of pathogen, and combinations thereof. In other embodiments the pathogen component is a pathogen and the probe is capable of binding to a pathogen.

(Spec. 6, l. 22 – 7, l. 6, emphasis added.) Thus, we agree with the Examiner that the Specification explicitly supports interpreting "pathogen" to include "pathogen fragments, pathogen nucleic acids, pathogen proteins, et cetera" (Ans. 37). Not only is the Examiner's interpretation consistent with intrinsic evidence in the Specification, it is consistent with extrinsic evidence of general usage in the art. *See* Ans. 10, *citing* DORLAND'S MEDICAL DICTIONARY, defining "pathogen" as "any disease-producing microorganism or material" (emphasis added).

In some embodiments, according to the Specification's explicit disclosure, a pathogen component is a pathogen. Because the claims recite "pathogen," not "pathogen component," we understand they are not directed to assaying for a non-disease-producing pathogen component. Instead, when the pathogen assayed for is a pathogen component, it is a "disease-producing" component as the DORLAND'S definition puts it. Whether a pathogen component assayed in a prior art reference was "disease-producing" is a question of fact, to be determined on a reference-by-reference basis.

ANTICIPATION

Principles of Law

> To anticipate a claim, a prior art reference must disclose every limitation of the claimed invention, either explicitly or

> inherently. Anticipation is an issue of fact, and the question whether a claim limitation is inherent in a prior art reference is a factual issue.

In re Schreiber, 128 F.3d 1473, 1477 (Fed. Cir. 1997) (citations omitted). "[T[he reference must be enabling and describe the applicant's claimed invention sufficiently to have placed it in the possession of a person of ordinary skill in the field of the invention." *In re Paulsen*, 30 F.3d 1475, 1478-79 (Fed. Cir. 1994). "[A]nticipation does not require actual performance of suggestions in a disclosure. Rather, anticipation only requires that those suggestions be enabling to one of skill in the art." *Bristol-Myers Squibb Co. v. Ben Venue Labs.*, 246 F.3d 1368, 1379 (Fed. Cir. 2001). The test for anticipation "is not an 'ipsissimis verbis' test." *In re Bond*, 910 F.2d 831, 832 (Fed. Cir. 1990).

B. Rejection over Rigler '903

Findings of Fact

4. With certain exceptions noted in the Analysis section below, we adopt the Examiner's findings of fact.

Analysis

Claim 59:

Appellants argue that Rigler analyzed molecules, not pathogens. (App. Br. 18.) The Examiner identified M13 DNA and *E. coli* as pathogens that Rigler assayed. M13 is a bacteriophage; bacteriophages inject their DNA into a bacterium; the DNA causes disease in the attacked bacterium. M13 DNA is a pathogenic component of M13, and is a pathogen according to Appellant's Specification. (Ans. 37-40.) There is no dispute that *E. coli* is a pathogen. The rejection on that point is supported by the evidence.

Appellants argue that Rigler did not assay fluctuations in fluorescence due to *E. coli* diffusion or flow through a subvolume. (App. Br. 19.) First, we find the evidence supports the Examiner's explanation that Rigler's FCS worked by measuring fluctuations in florescence. (*E.g.*, Ans. 34.) Appellants do not dispute that Rigler's M13 DNA was free to diffuse. Accordingly, we affirm the rejection of claim 59 and claims 118, 119, 124-126, 131 and 138 which were not separately argued. 37 C.F.R. § 41.37(c)(1)(vii).

Claim 60:

Appellants repeat their argument that Rigler discussed analyzing molecules, but "analyzing molecules does not constitute analyzing a pathogen—let alone analyzing fluctuations of fluorescence that are due to the diffusion or flow of a pathogen." (*Id.* at 20.) We disagree with that argument for the reasons given in the analysis of claim 59.

Appellants argue that Rigler did not teach a probe capable of binding a predetermined pathogen. (*Id.*) The Examiner cited Rigler at col. 13 and cols. 18-19 as evidence that Rigler did disclose such a probe. (Ans. 8.) The evidence supports the Examiner. We affirm the rejection of claim 60, and of its dependent claims 61-64, 122 and 123, which were not separately argued.

Claims 65, 66 and 130:

Claim 65 specifies that the "pathogen comprises a bacterium," claim 66 that the "pathogen comprises a virus," and claim 130 that the "pathogen comprises at least one of a bacterium and a virus." Appellants argue that Rigler did not teach analyzing fluorescence fluctuations that are due to the diffusion or flow of a bacterium through a subvolume. (App. Br. 21.) Appellants argue that Rigler at col. 6 "refers to the dwell time of a bacterium

in Rigler et al.'s measuring volume," but "[i]t cannot be disputed that the disclosure of a dwell time does not constitute an express teaching of analyzing fluctuations . . . due to the diffusion or flow of a bacterium through a subvolume." (*Id.*) We are not persuaded by Appellants' *ipsissimis verbis* argument because Rigler taught: "[w]hen a molecule migrates into said volume element by diffusion, it is excited and measured through the emitted light as long as it remains inside this measuring volume element. The average dwelling time is characteristic for the size and shape of a molecule, a molecular complex, or a cell." (Rigler, col. 13, ll. 5-10; *see* Ans. 8, referring Appellants to col. 12, l. 62 – col. 13, l. 10.)

The Examiner further rebutted these arguments by citing Rigler's col. 25 and 35 for teaching the FCS assay of bacteria and viruses (Ans. 9), and Rigler col. 21 for teaching "measurement of molecular and/or cellular mobilities (*id.* at 38, Examiner's emphasis). The evidence supports those findings. It is not necessary that an anticipating reference demonstrate actual performance of its teachings, only that they be enabled. *Bristol-Myers Squibb*, 246 F.3d at 1379. Thus, we are not persuaded that a particular example that measured dwell time negates in any way the Examiner's evidence that Rigler taught measuring cellular mobility, i.e., diffusion or flow. Appellants have not shown that Rigler did not enable its teachings. Claims 120 and 123:

Appellants argue that Rigler did not teach that the probe comprises multiple binding sites for the pathogen, as required by claims 120 and 123. (App. Br. 22.) The Examiner rebuts by citing Rigler, col. 37, as teaching "complexed ligands coupled to a fluorescence label, which read on a probe that includes multiple binding sites." (Ans. 42.) The cited passage appears

in Rigler's explanation of "Dynamic Laser Correlation Spectroscopy." We do not find an explicit disclosure of a probe with multiple binding sites, and the Examiner has not explained how that feature is implicit in the text. We reverse this rejection as not supported by the evidence of record.

Claim 121:

Appellants argue that Rigler did not teach a pathogen with multiple binding sites for the probe. (App. Br. 22.) The Examiner had cited Rigler's col. 12 disclosure of cross correlation of at least two "test reagents which will bind to different sequence segments of an analyte." (Ans. 9.) The Examiner rebutted Appellants' arguments by referring to the cols. 11-12 context of the disclosure. (Ans. 42.) The evidence supports the Examiner's findings.

Claim 127:

The Examiner cited Rigler's cols. 11-12 teachings of cross correlation and autocorrelation as evidence that claim 127 was anticipated. (Ans. 9.) Appellants contend that Rigler did "not teach obtaining a measured correlation function of a pathogen and applying a correlation algorithm to the measured correlation function" (App. Br. 22), but Appellants neither acknowledge nor rebut the Examiner's evidence. The Examiner responded to the argument by pointing to Rigler's specific col. 12 teaching that "[b]y means of a time cross correlation of the fluorescence signals . . . signals of the uncorrelated free test reagents can be efficiently suppressed at the level of electronic signal processing." (Ans. 42.) Because Appellant's argument does not address the Examiner's evidence, Appellants have not shown that the Examiner's reliance on Rigler's col. 11-12 disclosure was mistaken.

Claims 132 and 133:

Appellants contend that Rigler's anlaysis was done over a period no greater than 500 milliseconds, not over a period of seconds as claimed. (App. Br. 23.) The Examiner refers to Rigler's col. 7 and col. 23 disclosures. (Ans. 43-44.) The evidence does not support the rejection. We agree with Appellants that Rigler taught assaying over periods in the millisecond range and fractions of one second. We also agree with Appellants that the claim phrase "wherein the analyzing occurs over a period of seconds" is not reasonably interpreted to cover analyzing for periods less than a second. We therefore reverse the rejection of claims 132 and 133.

Claims 138, 62 and 118:

Appellants contend that the claims define a method requiring a "plurality of unique fluorescently tagged probes," "each unique probe capable of binding to a unique pathogen," a feature allegedly not taught by Rigler. (App. Br. 23-24.) The Examiner rebuts by pointing to Rigler's col. 11, ll. 33-44. (Ans. 45.) The evidence supports the Examiner.

C. Rejection over Rigler 1995

Findings of Fact

5. With certain exceptions noted in the Analysis section below, we adopt the Examiner's findings of fact.

Analysis

Claim 59:

Appellants contend that "[a] pathogen is an organism," and "[t]here is no evidence of record that M13 bacteriophage DNA, itself, produces a disease." (App. Br. 25.) However, the Specification defines pathogen to include a component of a pathogen, such as DNA. Appellants do not dispute that M13 bacteriophage DNA itself is the pathogen when the bacteriophage

attacks a bacterium; nor do Appellants allege that they require evidence to assess the nature of Rigler's M13 bacteriophage DNA. As the point is undisputed, the Examiner did not err by not burdening this record with unnecessary evidence.

Appellants argue that Rigler does not teach analyzing fluctuations of fluorescence due to a diffusion or flow of a pathogen through a subvolume. (*Id.*) First, we agree with the Examiner that FCS "is a long established procedure that measures fluctuations in fluorescence intensity." (Ans. 48.) Second, the evidence the Examiner cited supports the Examiner's finding that Rigler taught measuring fluorescence fluctuations from a small volume. (*Id.* at 12.) Third, the evidence the Examiner cited supports the Examiner's finding that Rigler taught fluctuation analysis and diffusion. (*Id.* at 52.)

Claim 60:

Appellants argue that Rigler did not teach a probe capable of binding a pathogen. (App. Br. 26.) In a section cited by the Examiner, titled "5. Diagnostics of pathogenic substances," Rigler taught: "[t]his can be achieved by hybridization of the vital [sic, viral] DNA with several fluorescence labeled primers." (Rigler, 182.) The example viruses Rigler named were hepatitis B and C, and HIV. (*Id.*) Plainly, Rigler was disclosing that the viral nucleic acid is among the "pathogenic substances" to be detected by FCS. Rigler's fluorescence labeled primers are Appellants' probes. The evidence supports the Examiner's findings.

Claims 66 and 130:

Appellants argue that "Rigler does not teach a virus," nor "analyze fluctuations of fluorescence that are due to the diffusion or flow of a virus through a subvolume," because Rigler instead teaches analyzing viral DNA

or RNA. (App. Br. 26-27.) The Examiner did not provide evidence on this point and we therefore reverse the rejection of claims 66 and 130.

Claims 120 and 123:

Appellants argue that "Rigler does not teach a probe that includes multiple binding sites for binding a pathogen." (App. Br. 27.) The Examiner did not provide evidence on this point and we therefore reverse the rejection of claims 120 and 123.

Claim 121:

Appellants argue that "Rigler does not teach a pathogen that includes multiple binding sites for binding the probe." (App. Br. 28.) We disagree. In the section cited by the Examiner, Rigler teaches "hybridization of the vital [sic, viral] DNA or RNA with several fluorescence labeled primers." (Rigler 182.) A pathogenic DNA or RNA hybridizable with several labeled primers necessarily includes multiple binding sites for the primers, i.e., probes.

Claim 127:

Appellants argue that "Rigler does not teach obtaining a measured correlation function of a pathogen and applying a correction algorithm to the measured correlation function." (App. Br. 28.) The Examiner did not provide evidence on this point and we therefore reverse the rejection of claim 127.

Claims 132 and 133:

Appellants argue that Rigler fails to teach analyzing over a period of seconds. (App. Br. 28-29.) The Examiner responds that Rigler disclosed analyzing over a period of milliseconds, and that "'period of seconds' encompasses time periods of less than one second." (Ans. 53.) We do not

agree that a period of plural seconds is reasonably interpreted to mean less than one second, and we reverse the rejection of claims 132 and 133.

Claims 138, 62 and 118:

Appellants argue that "Rigler does not teach a sample that includes a plurality of unique fluorescently tagged probes each of which is capable of binding to a unique pathogen." (App. Br. 29.) The Examiner has not provided evidence on this point and we therefore reverse the rejection of claims 138, 62 and 118.

D. Rejection over Weiner

The Issues

The Examiner's position is that Weiner taught "measuring serum hepatitis C virus (HCV) RNA, and [taught] a fluorescence correlation spectroscopy method (p. 85, Methods, para 7) for assaying the pathogen, HCV in a sample." (Ans. 15.)

Appellants contend that the RNA of hepatitis C virus is not a pathogen. (App. Br. 31.)

Findings of Fact

6. Weiner's paper is entitled "Rapid and Reproducible Quantification of Hepatitis C Virus cDNA by Fluorescence Correlation Spectroscopy." (Weiner.)
7. Weiner taught synthesizing cDNA and performing FCS on the synthetic cDNA. (*Id.* at 85, "Subjects and Methods.")

Analysis

Weiner determined serum HCV RNA by assaying for a synthetic proxy for the RNA, namely cDNA. (FF 7.) That is, the synthetic cDNA, not the RNA, was assayed by FCS. Synthetic cDNA has not been shown to

be a pathogen component. In contrast to HCV RNA, the disease causing agent in an RNA virus, there is no showing that Weiner's cDNA produces disease. Because cDNA is not a pathogen component, and there is no evidence that it produces disease, it does not meet the Specification's definition of a pathogen or a pathogen component that is a pathogen. The evidence does not support the rejection of Appellants' claims in all of which a pathogen is assayed by FCS.

E. Rejection over Walter

The Issue

The Examiner's position is that Walter taught "a method of assaying for the presence of a *Mycobacterium tuberculosis* pathogen component in a sample," the "sample comprising at least one primer … capable of binding a *M. tuberculosis* DNA pathogen component." (Ans. 18.)

Appellants contend that "Walter et al. do not teach a sample that includes a pathogen." (App. Br. 35.) According to Appellants, "[t]he genomic DNA of *Mycobacterium tuberculosis*, itself, does not produce a disease, and nothing in the record establishes anything to the contrary." (*Id.*)

Findings of Fact

8. Walter amplified genomic *M. tuberculosis* DNA by PCR. (Walter, 12806, "PCR in the Presence of Probes.")
9. In Walter's method, "[a]fter PCR, a 10-µl sample of the reaction mixture was applied without further manipulation to the water immersion 63 x 1.2 microscope objective of a FCS setup." (*Id.*, "FCS Measurement and Extraction of Relative Diffusion Times.")

Analysis

Walter performed FCS on a sample of the reaction mixture from PCR amplification of *M. tuberculosis* genomic DNA. (FF 9.) Appellants argue that genomic *M. tuberculosis* DNA does not produce a disease, and is not a pathogen. In response, the Examiner agrees that a pathogen must be "disease-producing," but offers no evidence that Walter's genomic DNA is disease-producing. (Ans. 66, *citing* DORLAND'S.) We agree that the genomic DNA is a pathogen component, but in the absence of evidence that it is disease-producing, we cannot find that it is a pathogen. We therefore reverse this rejection.

OBVIOUSNESS

Principles of Law

When determining whether a claim is obvious, an Examiner must make "a searching comparison of the claimed invention – including all its limitations – with the teaching of the prior art." *In re Ochiai*, 71 F.3d 1565, 1572 (Fed. Cir. 1995).

Findings of Fact

10. With certain exceptions noted in the Analysis section below, we adopt the Examiner's findings of fact.

Analysis

Claim 59:

The Examiner's position is that Kask taught an FCS method for detecting substances in a sample, and that Kask's method corresponded to Appellants but for the fact that Kask did not teach applying the method to detecting "pathogens." (Ans. 21-22.) The Examiner found that Lahiri taught the detection of pathogens, and taught using FCS for that purpose.

The Examiner found that because Kask taught high throughput screening, diagnostic purposes, and assaying for bacteria and viruses, and because Lahiri taught using FCS for detecting pathogens such as bacteria and viruses, one of ordinary skill in the art would have been motivated to apply FCS to pathogen detection. (*Id.* at 23.) Based on those findings, the Examiner concluded it would have been obvious to use Kask's FCS method to detect pathogens, including the viruses and bacteria that Lahiri taught. (*Id.*)

Appellants contend that Kask did "not teach analyzing the fluctuations in fluorescence due to the diffusion or flow of a pathogen through a subvolume," and characterizes Kask as providing "a laundry list of examples of 'units,' which includes "particles, molecules, aggregates, vesicles, cells, viruses, bacteria, ..." (App. Br. 41-42.) Appellants discount Kask's claims that mention a bacteria or a virus because those claims "do not state that the bacteria or virus is the molecule or particle referred to in the independent claim from which it depends." (*Id.* at 43.) Appellants contend that the fact that some claims of Kask mention fluctuations is irrelevant. (*Id.*) According to Appellants, "[n]one of the examples of Kask involve analyzing bacteria or viruses, in general, or analyzing the diffusion or flow of a bacterium or virus, in particular." (*Id.*) According to Appellants, Lahiri did not teach a sample that included a pathogen, and Lahiri focused on membrane arrays, and immobilizing pathogens on the arrays. (*Id.* at 44.)

We find that Appellants' arguments do little more than urge us to ignore the teachings of the references. This we cannot do. We conclude that the facts in evidence support a prima facie case of obviousness, and that Appellants' contentions do not rebut it.

Claims 62 and 118:

Appellants contend that neither reference taught a sample that includes a plurality of unique fluorescently tagged probes, each probe comprising a unique fluorophore, each unique probe being capable of binding a unique pathogen. (App. Br. 45.) The Examiner rebuts by pointing to Kask's disclosure of assaying for plural targets, including Lahiri's pathogens. (Ans. 76-77.) The Examiner further rebuts by pointing to Kask's Example 2 and screening disclosures. (*Id.* at 79-80.) We agree that the evidence supports the Examiner's position that it would have been obvious to a person of ordinary skill in the art to apply those teachings to assay for plural pathogenic targets, using plural tagged probes specific for the various targets.

Claims 120 and 123:

Appellants contend that the combined references do not teach or suggest a probe that includes multiple binding sites for binding a pathogen. (App. Br. 45.) The Examiner rebuts by pointing to Lahiri's teaching to "use labeled antibodies … for bound target, which describes probes for multiple binding sites" on the target. (Ans. 81, citing Lahiri [0072].) When Lahiri's target is assayed for in Kask's method, we agree that it would have been obvious to continue using the labeled antibodies for the bound target.

Claim 121:

Appellants argue that the combined references do not teach or suggest a pathogen that includes multiple binding sites for the probe. (App. Br. 46.) The Examiner cited Kask at col. 8. (Ans. 22.) Kask's col. 8 discloses a plurality of fluorescently tagged probes for a single pathogen, i.e., a primer "cocktail" for a target nucleic acid molecule. We agree with the Examiner

that this evidence supports the conclusion that it would have been obvious to assay for a pathogenic nucleic acid, such as a viral nucleic acid by Kask's method using a cocktail of tagged primers.

Claim 127[8]:

Appellants argue that the combined references do not teach or suggest obtaining a measured correlation function of a pathogen and applying a correction algorithm to the measured correlation function. (App. Br. 46.) The Examiner rebuts by pointing to Kask's col. 13 disclosure said to "teach brightness corrected fluorescence correlation spectroscopy data, which reads on obtaining a measured correlation function of a pathogen and applying a correction algorithm to the measured correlation function." (Ans. 82.) The evidence supports the Examiner's finding.

Claims 132-137:

Appellants argue that the combined references do not teach or suggest analyzing fluorescence fluctuations over a period of seconds. (App. Br. 47.) The Examiner rebuts by pointing to Kask's col. 12 disclosure of working examples with 40 second duration. (Ans. 82.) Given this evidence, we agree it would have been obvious to a person having ordinary skill in the art to conduct measurements over an appropriate period of time, including a period of seconds.

Claim 138:

Appellants contend that neither reference taught a sample with a plurality of unique fluorescent probes, each unique probe including a unique fluorophore, each unique probe being capable of binding to a unique

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[8] Appellants presented an argument about claim 126 (App. Br. 46), but claim 126 was not rejected for obviousness.

pathogen, and that the combination thus lacks a required element of the claim. (App. Br. 47-48.) We disagree. The Examiner rebutted this argument by pointing to Kask's teachings concerning plural analytes, discussed above for claim 62 and 118.

SUMMARY

We reverse the rejection of claims 132-137 under 35 U.S.C. § 112, 1st paragraph.

We reverse the rejection of claims 59, 118-121, 124-126, 130-132, 134 and 136 under 35 U.S.C. § 112, 2nd paragraph.

We reverse the rejection of claims 131-133 under 35 U.S.C. § 112, 2nd paragraph.

We affirm the rejection of claims 59, 60-64, 118, 119, 122, 124-127, 131 and 138 under 35 U.S.C. § 102(e) as anticipated by Rigler '903.

We reverse the rejection of claims 120, 123, 132 and 133 under 35 U.S.C. § 102(e) as anticipated by Rigler '903.

We affirm the rejection of claims 59-61, 63, 64, 119, 121, 122, 124, 125, 128 and 131 under 35 U.S.C. § 102(b) as anticipated by Rigler, Journal of Biotechnology ("Rigler 1995").

We reverse the rejection of claims 62, 66, 118, 120, 123, 127, 130, 132, 133 and 138 under 35 U.S.C. § 102(b) as anticipated by Rigler, Journal of Biotechnology ("Rigler 1995").

We reverse the rejection of claims 59-64, 66, 118-125, 127, 128 and 130-138 under 35 U.S.C. § 102(b) as anticipated by Weiner.

We reverse the rejection of claims 59-65, 118-125, 127, 128 and 130-138 under 35 U.S.C. § 102(b) as anticipated by Walter.

We affirm the rejection of claims 59-66, 118-125, 127, 128 and 130-138 under 35 U.S.C. § 103(a) as unpatentable over Kask and Lahiri.

37 C.F.R. § 41.50(b)

Several of the affirmed rejections are based on evidence first cited in the Examiner's Answer "Response to Argument" section. Because that evidence is new to those particular rejections, we designate the affirmances as new grounds of rejection.

This decision contains a new ground of rejection pursuant to 37 CFR § 41.50(b) (effective September 13, 2004, 69 Fed. Reg. 49960 (August 12, 2004), 1286 Off. Gaz. Pat. Office 21 (September 7, 2004)). 37 CFR § 41.50(b) provides "[a] new ground of rejection pursuant to this paragraph shall not be considered final for judicial review."

37 CFR § 41.50(b) also provides that the appellants, WITHIN TWO MONTHS FROM THE DATE OF THE DECISION, must exercise one of the following two options with respect to the new ground of rejection to avoid termination of the appeal as to the rejected claims:

> (1) *Reopen prosecution.* Submit an appropriate amendment of the claims so rejected or new evidence relating to the claims so rejected, or both, and have the matter reconsidered by the Examiner, in which event the proceeding will be remanded to the Examiner. . . .
>
> (2) *Request rehearing.* Request that the proceeding be reheard under § 41.52 by the Board upon the same record. . . .

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED-IN-PART; 37 C.F.R. § 41.50(b)

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